DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

The Derbyshire commissioning guidelines for the treatment of severe psoriasis in adults

This algorithm is a tool to aid the implementation of NICE guidance on biologic drugs for the treatment of psoriasis. It includes all of the biologic drugs approved by NICE for treatment and local variations for the commissioning algorithm.

Severe Psoriasis: **PASI ≥ 10 and DLQI > 10 and failed previous systemic therapies or these treatments are CI or not tolerated** (e.g. ciclosporin, methotrexate or PUVA (psoralen and long-wave ultraviolet radiation))

Apremilast (TA419) or
Dimethyl Fumarate (TA475)

For dosing see - appendix 2
Adequate response* within 16 weeks

No

Yes

Maintain same treatment and monitor patient (adequate response time 16 weeks)

Yes – consider alternative biologic agent – (local agreement)

If more than 1 treatment is suitable, the least expensive should be chosen.
Choices are listed in most cost effective order.

- Adalimumab biosimilar (TNFi) (TA146) or
- Tildrakizumab (IL23) (TA575) or
- Bimekizumab (IL17A &17F &17AF) (TA723) or
- Risankizumab (IL23) (TA596) or
- Etanercept biosimilar (TNFi) (TA103) or
- Ixekizumab (IL17A) (TA442) or
- Guselkumab (IL23) (TA521) or
- Brodalumab (IL17RA) (TA511) or
- Secukinumab (IL17A) (TA350) or
- Certolizumab (TNFi) (TA574) or
- Ustekinumab (IL12 & IL23) (TA180)

Or

- **Infliximab biosimilar (TNFi) (TA134)**

Has the biologic been withdrawn because of an adverse effect?

No

- If no adequate response at specified time (see appendix 1) - the patient is a **primary non-responder or**
- **secondary non-responder** (initially responds, but subsequently loses response), proceed as per local guidance below

The CCG's will only commission 2 treatment options (1 switch) per patient. JAPC recognises the RMOC statement. Further sequential use outside of the commissioning algorithm should be undertaken after advice via MDT in-line with Trust processes but is limited by clinical appropriateness and safety.

Reassess PASI and DLQI if the patient fails to respond to the first biologic.
Proceed to second biologic if:

- **PASI >15 and DLQI>15 and**
- **the patient has had a 6 week trial of topical treatment and**
- **there is a risk of admission within the 6 weeks and**
- **Requests are sent to** the CCG through Blueteq

Adequate response defined as:
**a 75% reduction in the PASI score (PASI 75) from when treatment started*
or
a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in the DLQI score from when treatment started.

Previous drug treatment an interleukin mediated biologic:

- Ixekizumab (IL17A) non-responder
- Brodalumab (IL17RA) non-responder
- Secukinumab (IL17A) non-responder
- Bimekizumab (IL17A &17F &17AF) non-responder
- Risankizumab (IL23) non-responder
- Tildrakizumab (IL23) non-responder
- Guselkumab (IL23) non-responder
- Ustekinumab (IL12 & IL23) non-responder

Second drug option:

- Adalimumab biosimilar
- Etanercept biosimilar
- Certolizumab
- Infliximab biosimilar (very severe psoriasis)

Previous drug treatment with:

- Adalimumab biosimilar non-responder
- Infliximab biosimilar non-responder
- Etanercept biosimilar non-responder
- Certolizumab non-responder

Second drug option:

- Ixekizumab (IL17A)
- Brodalumab (IL17RA)
- Secukinumab (IL17A)
- Bimekizumab (IL17A &17F & 17AF)
- Risankizumab (IL23)
- Tildrakizumab (IL23)
- Guselkumab (IL23)
- Ustekinumab (IL12 & IL23)

Local variation to NICE

NICE approved treatment

In exceptional circumstances some patients may not show adequate response to a second biologic, **and** the psoriasis may have worsened (PASI>15 and DLQI>15,) **and** there may be a risk of readmission; under these circumstances it may be appropriate to request the use of a third biologic through from a tertiary centre (See appendix 1 for further details)

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Appendix 1

Use of third biologic – through a tertiary centre

For patients who have not had an adequate response to a second biologic and the psoriasis has worsened (PASI>15 and DLQI>15) and there is a risk of readmission, use of a third biologics can be considered if

1. Approved by an MDT at a tertiary centre
2. The biologic prescribed is of a different mode of action to the previously tried therapies
3. Request is submitted to the CCG through Blueteq

Appendix 2

Biologic	Type	Route	Dose	Adequate response (weeks)	Further information
Infliximab biosimilar	Chimeric human-murine IgG1 monoclonal antibody	IV	5mg/kg at week 0,2,6, thereafter every 8 weeks	10	Reserved for people with severe disease as per the NICE TA.
Etanercept biosimilar	Recombinant human tumour necrosis factor (TNF) receptor fusion protein that inhibits the activity of TNF	SC	**25mg twice weekly**. Alternatively **50mg twice weekly** may be used for **up to 12 weeks** followed, if necessary, by a dose of **25 mg twice weekly**	12	NA
Adalimumab biosimilar	Recombinant human monoclonal antibody that binds specifically to tumour necrosis factor alpha (TNF-α).	SC	Initial 80 mg dose, followed by 40 mg given every other week starting 1 week after the initial dose	16	Ideal first line for patients with associated psoriatic arthritis
Secukinumab	High-affinity, fully human Monoclonal antibody that binds to and neutralises interleukin-17A.	SC	300mg at weeks 0, 1, 2 & 3, followed by monthly maintenance dosing starting at week 4	12	Useful for patients at high risk of demyelinating disease or TB. Useful for patients requiring high level of clinical response
Ixekizumab	Antibody that inhibits IL-17A (interleukin-17A, a pro-inflammatory cytokine).	SC	160 mg at week 0, followed by 80 mg every 2 weeks until week 12. After week 12, 80 mg every 4 weeks	12	Useful for patients at high risk of demyelinating disease or TB. Useful for patients requiring high level of clinical response
Ustekinumab	Fully human monoclonal antibody that targets interleukin-12 (IL-12) and IL-23	SC	Weight ≤ 100kg - 45 mg for, Weight >100kg – 90mg Administered at week 0 followed by another dose at week 4, and then a further dose every 12 weeks	16	Ustekinumab has better drug survival rates and a now well established safety record. BAD advises as a potential first line agent in absence of psoriatic arthritis.
Brodalumab	Recombinant fully human monoclonal immunoglobulin IgG2 antibody that binds with high affinity to human IL-17RA and blocks the biological activities of the pro-inflammatory cytokines IL-17A, IL-17F, IL-17A/F heterodimer and IL-25.	SC	210 mg at weeks 0, 1 and 2, followed by 210 mg every 2 weeks	12	Useful second line agent in patients who fail an initial biological agent or for patients at high risk of demyelinating disease or TB. Useful for patients requiring high level of clinical response
Guselkumab	Guselkumab is a human IgG1λ monoclonal antibody (mAb) that binds selectively to the interleukin 23 (IL-23) protein with high specificity and affinity.	SC	100 mg by at weeks 0 and 4, followed by a 100 mg maintenance dose every 8 weeks.	16	NA

Certolizumab	Certolizumab binds specifically to tumour necrosis factor alpha (TNF-α).	SC	Loading dosage: 400 mg (given as 2 x200 mg each) at weeks 0, 2 and 4. Maintenance dosage: 200 mg every 2 weeks.	16	Studies have shown there is no to minimal placental transfer of Certolizumab from mothers to infants. Certolizumab may be a useful option for patients willing to be become pregnant.
Tildrakizumab	Humanized IgG1/k monoclonal antibody that specifically binds to the p19 protein subunit of the interleukin-23 (IL-23) cytokine without binding to IL-12 and inhibits its interaction with the IL-23 receptor.	SC	100 mg at weeks 0 and 4 and every 12 weeks thereafter. In patients with certain characteristics (for example, high disease burden, body weight of 90 kg or more), a 200 mg dose may provide greater efficacy.	28	NA
Risankizumab	Humanised IgG1 monoclonal antibody that binds to and neutralises the p19 subunit of interleukin-23	SC	150mg at weeks 0 and 4 and every 12 weeks thereafter.	16	NA
Bimekizumab	Humanised IgG1 monoclonal antibody that selectively inhibits IL-17F and IL17A, 17AF	SC	320mg (2x160mg) by SC injection at week 0 - 320mg week 4 - 320mg week 8 -320mg week 12 - 320mg week 16 - 320mg and thereafter every 8 weeks	16	Patients with a body weight of 120kg or more who did not have complete skin clearance at week 16 may improve further by increasing their dosage to 320 mg every 4 weeks.

Appendix 3

Dose titration for Dimethyl Fumarate

To improve tolerability, it is recommended to begin treatment with a low initial dose with subsequent gradual increases. The maximum daily dose allowed is 720 mg (3 x 2 tablets of dimethyl fumarate 120 mg).

Week	Number of tablets			Total daily dose (mg) of dimethyl fumarate
	Morning	Midday	Evening	
Dimethyl fumarate 30 mg				
1	0	0	1	**30**
2	1	0	1	**60**
3	1	1	1	**90**
Dimethyl fumarate 120 mg				
4	0	0	1	**120**
5	1	0	1	**240**
6	1	1	1	**360**
7	1	1	2	**480**
8	2	1	2	**600**
9+	2	2	2	**720**

Dose titration for apremilast

- Day 1 - 10mg am
- Day 2 - 10mg am & pm
- Day 3 - 10mg am, 20mg pm
- Day 4 - 20mg am & pm
- Day 5 - 20mg am & 30mg pm
- Day 6 and thereafter - 30mg am & pm

NB: reduce dose 30mg od in severe renal impairment (CrCl <30ml/min, estimated using Cockcroft-Gault equation)

MHRA warning - apremilast

MHRA, Jan 2017, have issued a warning regarding risk of suicidal thoughts and behavior associated with apremilast use.